REMARKS

Applicant respectfully requests entry of the Amendment and reconsideration of the claims. Claims 105, 115, and 123 have been amended. Applicant currently amends claim 123 to correct an obvious typographical error. Applicants submit that the claims as amended are supported throughout the specification including at page 59, lines 23-25; page 100, lines 5-15; and page 107, lines 18-28.

Claims 105-107, 109-111, and 113-128 are pending. Claims 1-7, 9-12, 15-24, 29-34, 36-40, 42, 44-46, 48-54, 59-66, 68-74, 76, 81-85, 90-96, 98-99, 108, 112, and 129-130 are withdrawn. Applicants request rejoinder of these claims after notice of allowable subject matter of claim 105.

Priority

The Examiner objects to the claim for the benefit of priority and contends that provisional applications 60/441,059 filed 1/16/2003, 60/488,610 filed July 18, 2003, and 60/510,314 filed October 8, 2003 do not provide support for a CDRH3-phage coat fusion protein comprising a "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural". The Examiner further asserts that a fusion protein comprising at least a portion of a phage coat protein is not supported in the earlier applications as well. Applicants respectfully disagree with the Examiner and request acknowledgement of the claim for priority of the currently pending claims. We further understand the examiner's rejection to be based on a 112 rejection. Applicants traverse this rejection.

The written description requirement requires that Applicants' specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). A written description of an invention involving a chemical genus requires a precise definition, such as by structure, formula ... of the claimed subject matter sufficient to distinguish it from other materials. Univ. of California v. Eli Lilly and Co., 43 USPQ2d 1398. 1405 (Fed. Cir. 1997) (emphasis added). Since one skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass, such a formula is

normally an adequate description of the claimed invention. Id. at 1406 (emphasis added). there is a "strong presumption" that an adequate written description of the claimed invention is present when the application is filed. In re Wertheim, 191 USPQ 90,97 (CCPA 1976). Compliance with the written description requirement does not require an applicant to describe exactly the subject matter claimed; rather, the description must clearly allow a person of ordinary skill in the art to recognize that he or she invented what is claimed. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The test is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that applicant had possession of the subject matter later claimed. In re Kaslow, 217 USPQ 1089 (Fed. Cir. 1991). Moreover, in order to have possession of members of a claimed genus, the specification need not describe all of the species that the genus encompasses. Amgen Inc. v. Chugai Pharmaceutical Co., 18 USPQ2d 1016, 1027 (Fed. Cir. 1991).

Applicants claim 105 is now directed to a fusion protein comprising at least a portion of a filamentous phage coat protein fused to a binding polypeptide comprising a heavy chain variable domain comprising a CDRH3 scaffold comprising: a) an N-terminal portion of 1 to 4 amino acids in which some or all amino acid positions are structural; b) a C terminal portion of 1 to 6 amino acids in which some or all amino acid positions are structural, and c)a central portion or loop of 1 to 20 contiguous amino acids that can vary in sequence and in length, wherein the portion of the phage coat protein provides for display of the fusion protein on the filamentous phage.

On page 3 of the Office Action, the Examiner contends that the support for a "N-terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and "a C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural" are not disclosed in the earlier applications. As we understand it, the examiner is raising an issue with respect to the term "about" based on the emphasis placed on those words at page 4 of the Office Action. While not acquiescing to the rejection and solely to expedite prosecution, Applicants claims no longer recite "about".

As discussed previously, Applicants submit that the priority documents disclose the currently claimed subject matter. Applicants direct the Examiner's attention to Figures 45 and 46 of the provisional 60/441,059 (filed January 16, 2003). In addition, many other portions of the

specification provide support including at page 18 of the provisional 60/441,059 (filed January 16, 2003):

> "In one embodiment, structural amino acid positions in a CDRH3 are typically located near the N and C terminus of the CDRH3. Structural amino acid positions are selected from the group consisting of the first N-terminal amino acid, the second N-terminal amino acid and **at least one of the last 6 amino acids at the C-terminus of a heavy chain CDRH3**. In another embodiment, at least one structural amino acid position is one or both of the first two amino acid positions at the N-terminus of a heavy chain CDRH3. In another embodiment, **said at least one structural amino acid position is a third and/or fourth amino acid position from the C-terminus**."
>
> At page 21:
> "A library of randomly generated 17 amino acid CDRH3 indicated that a consensus sequence R-L-R at the N-terminus may be preferred for some embodiments."
>
> The examples indicate at page 107:
>
> "Finally, we combined the above two analysis, positional and by residue type, to determine those amino acids and those positions which were significantly over represented (Figure 45). Positions 96(Arg), 97(Leu), 99(Arg),102a (Gly), 102b (Gly), **102e(Trp), 102f(Phe), 102h(Val), and 102j (Val)** show a significant deviation from random (one and a half standard deviations or greater) for both preference of amino acid type at that position and bias for that position for any given residue as compared to the distribution of that amino acid along the entire 17 residue loop. These amino acid preferences indicate that certain amino acids are preferred at these positions, and that these positions are more likely to play a structural role in CDRH3."

Applicants submit that these passages as well as figures 45 and 46 provide for support and priority for claim 105. It is clear that the specification of the priority document describes a CDRH3 phage coat protein fusion protein (see underline) comprising a " N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural". Please see underlined sections above and Figures 45 and 46. It is also clear that the specification of the priority document also describes and supports a "C terminal portion of about 1 to 6 amino acids in which some or all of the amino acid positions are structural". See bold sections above. Applicants respectfully request acknowledgement of priority of the currently pending claims to provisional application 60/441,059 filed January 16, 2003.

Moreover, similar support can be found in the provisional application 60/488,610 filed July 18, 2003. For example, at page 18 of the provisional, the application states:

"In one embodiment, structural amino acid positions in a CDRH3 are located near the N and C terminus of the CDRH3. For example, in a 17 amino acid CDRH3 region, structural amino acid positions are selected from the group consisting of the first N-terminal amino acid, the second N-terminal amino acid, **at least one of the last 6 amino acids at the C-terminus of a heavy chain CDRH3 or mixtures thereof.** In another embodiment, at least one structural amino acid position is one or both of the first two amino acid positions at the N-terminus of a heavy chain CDRH3. In another embodiment, **said at least one structural amino acid position is a third , fourth and/or sixth amino acid position from the C-terminus."**

At page 22,

"Another embodiment of a CDRH3 region comprises an amino acid sequence R-L/I/M-A_3-R-$(A_5)_n$, wherein A_3 and A_5 are any naturally occurring amino acid and n is 1 to 20. A library of randomly generated 17 amino acid CDRH3 indicated that a consensus sequence R-L/I/M- A_3-R at the N-terminus may be preferred for some embodiments."

At page 109,

"Amino acids that deviated most significantly from random ($p<0.05$) showed a strong selection bias for particular amino acids at certain positions in the CDRH3 peptide. The N terminal end of the peptide was biased towards the sequence motif R(L/I/M)XR. Near the central portion of the peptide, the preference seemed to be for either glycine or hydrophilic residues. The C-terminal end of CDR3 (positions 102e-102j) was characterized by an over representation of hydrophobes (Phe, Val, Ile and Trp) at particular positions."

At page 113,

"These results indicate that amino acids located at the N and C-terminus of CDRH3 should be less diversified than other amino acids. Structural amino acid positions were identified as those positions that had a ratio of wild type amino acid to alanine of at least about 3 to 1 or greater and more preferably, about 10 to 1 or greater. The structural amino acid positions identified in the analysis include the first two N-terminal amino acid positions (positions 96 and 97 in this example) and **one or more of the last 6 amino acid positions located at the C-terminus in the 17 amino acid peptide of CDRH3 (positions 102e, 102f, 102g, 102h, 102i and 102j)**."

Applicants submit that these passages as well as figure 45 provide for support and priority for claim 105. It is clear that the specification of the priority document describes a CDRH3 phage coat protein fusion protein comprising an "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural". Please see underlined sections above and Figure 45. It is also clear that the specification of the priority document also describes and

supports a "C terminal portion of about 1 to 6 amino acids in which some or all of the amino acid positions are structural". See bold sections above. Applicants request acknowledgement of priority of the currently pending claims to provisional application 60/488,610 filed July 18, 2003.

The Examiner also contends that "at least a portion of a phage coat protein" lacks support in the priority documents. The examiner contends that " a portion of the phage coat protein" reads on a single amino acid and further that the phage coat protein is essential material. Applicants disagree.

While not acquiescing to the rejection and solely to expedite prosecution, Applicants have amended claim 105 to refer to filamentous phage coat protein and wherein the portion of the phage coat protein provides for display of the fusion protein on the filamentous phage. The support for this amendment in the priority document, provisional 60/441,059 (filed January 16, 2003), is found throughout the specification including at page 33, lines 19-31:

> "Phage display" is a technique by which variant polypeptides are displayed as fusion proteins to a coat protein on the surface of phage, *e.g.*, filamentous phage, particles. A utility of phage display lies in the fact that large libraries of randomized protein variants can be rapidly and efficiently sorted for those sequences that bind to a target molecule with high affinity. Display of peptide and protein libraries on phage has been used for screening millions of polypeptides for ones with specific binding properties. Polyvalent phage display methods have been used for displaying small random peptides and small proteins through fusions to either gene III or gene VIII of filamentous phage. Wells and Lowman, *Curr. Opin. Struct. Biol.,* 3:355-362 (1992), and references cited therein. In monovalent phage display, a protein or peptide library is fused to a gene III or a portion thereof, and expressed at low levels in the presence of wild type gene III protein so that phage particles display one copy or none of the fusion proteins.

At page 68, lines 11-16:

> "Examples of viral coat proteins include infectivity protein PIII, major coat protein PVIII, p3, Soc, Hoc, gpD (of bacteriophage lambda), minor bacteriophage coat protein 6 (pVI) (filamentous phage; J Immunol Methods. 1999 Dec 10;231(1-2):39-51), variants of the M13 bacteriophage major coat protein (P8) (Protein Sci 2000 Apr; 9(4):647-54). The fusion protein can be displayed on the surface of a phage and suitable phage systems include M13KO7 helper phage, M13R408, M13-VCS, and Phi X 174, pJuFo phage system (J Virol. 2001 Aug; 75(15):7107-13.v), hyperphage (Nat Biotechnol. 2001 Jan; 19(1):75-8)."

Applicants submit that the portion of the filamentous phage coat protein is not essential material as the sequences and the portions of phage coat proteins that provide for phage

display are known to those of skill in the art and are available in publicly available databases. Applicants provide one such reference attached hereto. In addition, Applicants have provided publicly available references as described above. In addition, Applicants' specification provides the nucleic acid sequence of a portion of the M13 p3 phage coat protein in Figures 15, 16, 17, and 18. For example, in Figure 15, the start of p3 is at nucleotide 965 and the end is shown at nucleotide 1439. This corresponds to about 158 amino acids of the C terminal end of the p3 protein as described at page 99, lines 10-15:

> "Vectors encoding fusion polypeptides comprising variant CDRs were constructed as follows. In general, vectors for antibody phage display were constructed by modifying vector pS1602 (Sidhu et al., J. Mol. Biol. (2000), 296:487-495). Vector pS1602, which has pTac promoter sequence and *malE* secretion signal sequence, contained a sequence of human growth hormone fused to the C-terminal domain of the gene-3 minor coat protein (p3)."

Applicants submit that they have sufficiently described the portion of phage coat proteins by providing publicly available sources for the sequences of the phage coat proteins, and describing at least one embodiment of the C terminal portion of the M13 p3 protein. As the Board of Appeals indicated in Ex parte Rios at page 7,

> "[W]hat is needed to support generic claims to biological subject matter depends on a variety of factors , such as existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter…"

Applicants submit that the Examiner has not provided any evidence that one of skill in the art would not have been in possession of at least a portion of a phage coat protein given the disclosure in the specification as well as the knowledge in the art.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the objection to the claim to priority.

Rejection under 35 U.S.C. § 102(a)

The Examiner rejects claims 105-107, 109, 111, 113, and 115-128 under 35 U.S.C. § 102(a) as allegedly anticipated by Bond et al. (*J. Mol. Biol.*, 332:643-655 (2003)). Applicant respectfully traverses this rejection.

Applicants submit that the pending claims are entitled to a priority date of at least Jan. 16, 2003 and July 18, 2003 (see argument above). The Bond et al. paper was published on

September 19, 2003, and Applicant respectfully asserts that it is therefore not properly considered prior art to the instant application.

Applicant respectfully requests removal of the rejection under 35 U.S.C. § 102(a).

Rejection under 35 U.S.C. § 112, First Paragraph

The Examiner rejects claims 105-107, 109-111, and 113-128 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner contends that the rejected limitations are new matter. The examiner contends that there is no support for a portion of a phage coat protein, for a hydrophobic amino acid residue at position 45, and no support for two framework regions. Applicants respectfully traverse.

Under 35 U.S.C. §112, first paragraph, a patent specification must contain sufficient written description in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention (*Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991)). "The specification must teach the invention by describing it." (*Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004)).

At least a portion of a phage coat protein. The Examiner rejects claim 105 for reciting "at least a portion of a phage coat protein". Applicant respectfully asserts that "at least a portion of a phage coat protein" is described throughout the specification, including at page 11, lines 3-4; page 18, lines 8-9; page 55, line 28 to page 56, line 6; page 88, lines 12-13; and page 99, lines 29-31. At page 100, lines 5-15, the specification provides further description.

> [A] fusion protein comprises an antibody variable domain…fused to all or a portion of a viral coat protein. Examples of viral coat proteins include infectivity protein PIII, major coat protein PVIII, p3, Soc, Hoc, gpD (of bacteriophage lambda), minor bacteriophage coat protein 6 (pVI) (filamentous phage; J Immunol Methods. Dec. 10, 1999;231(1-2):39-51), variants of the M13 bacteriophage major coat protein (P8) (Protein Sci April 2000; 9(4):647-54). The fusion protein can be displayed on the surface of a phage and suitable phage systems include M13KO7 helper phage, M13R408, M13-VCS, and Phi X 174, pJuFo phage system (J Virol. August 2001; 75(15):7107-13.v), hyperphage (Nat Biotechnol. January 2001; 19(1):75-8). The preferred helper phage is M13KO7, and the preferred coat protein is the M13 Phage gene III coat protein.

Applicants submit that the portion of the filamentous phage coat protein is described in the specification and are known to those of skill in the art as the sequences and the portions of phage coat proteins that provide for phage display are available in publicly available databases. Applicants provide one such reference attached hereto. In addition, Applicants have provided publicly available references as described above. The working examples provide detailed description of fusion proteins as well as how to make a fusion protein comprising at least a portion of a phage coat protein.

In addition, Applicants' specification provides the nucleic acid sequence of a portion of the M13 p3 phage coat protein in Figures 15, 16, 17, and 18. For example, in Figure 15, the start of p3 is at nucleotide 965 and the end is shown at nucleotide 1439. This corresponds to about 158 amino acids of the C terminal end of the p3 protein as described at page 99, lines 10-15:

> "Vectors encoding fusion polypeptides comprising variant CDRs were constructed as follows. In general, vectors for antibody phage display were constructed by modifying vector pS1602 (Sidhu et al., J. Mol. Biol. (2000), 296:487-495). Vector pS1602, which has pTac promoter sequence and *malE* secretion signal sequence, contained a sequence of human growth hormone fused to the C-terminal domain of the gene-3 minor coat protein (p3)."

Applicants submit that they have sufficiently described the portion of phage coat proteins by providing publicly available sources for the sequences of the phage coat proteins, and describing at least one embodiment of the C terminal portion of the M13 p3 protein. As the Board of Appeals indicated in Ex parte Rios at page 7,

> "[W]hat is needed to support generic claims to biological subject matter depends on a variety of factors , such as existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter…"

Applicants submit that the Examiner has not provided any evidence that one of skill in the art would not have been in possession of at least a portion of a phage coat protein given the disclosure in the specification as well as the knowledge in the art. For at least this reason, Applicant respectfully asserts that the specification fully describes "at least a portion of a phage coat protein."

Any hydrophobic amino acid. The Examiner rejects claim 123 and alleges that the "residue at framework position 45 may be any hydrophobic amino acid" lacks written description. Applicant respectfully traverses.

The specification supports the recitation of framework position 45 being wild-type arginine or any hydrophobic amino acid. Specifically, support for this claim can be found in Example 14 at pages 163-164 of the specification and in Figure 40. Figure 40 shows the preference for hydrophobic amino acids at that position including phe, leu, trp, val, met and tyr. At page 86, line 30 to page 87, line 5, the specification states:

> "The hydrophobic amino acids are preferably selected from the group consisting of leucine, isoleucine, valine, tryptophan, tyrosine, and phenylalanine. In a VHH variable domain, the structural amino acids positions in a CDRH3 are preferably substituted with hydrophobic amino acids to stabilize the VHH in the absence of the light chain at the former light chain interface."

The specification at page 163, line 31 to page 164, line 4 recites:

> Aside from Arg, **both domains preferred hydrophobic residues at position 45 and** the RIG domain in particular contained a substantial proportion of Trp, Phe and Leu residues. Overall, these results demonstrate that changes at positions 37 and 45 of V_HH domains relative to V_H domains contribute to protein stability, as they allow for favorable hydrophobic interactions amongst themselves and with CDR3. See Figure 52. emphasis added

For at least this reason, Applicant respectfully asserts that "any hydrophobic amino acid" at framework region position 45 is fully described by the specification.

Another framework region. The Examiner rejects claim 126 due to the recitation of "another framework region." Applicant respectfully traverses.

Claim 123 recites "a framework region that comprises a hydrophobic amino acid at position 37 and an amino acid at position 45 selected from…" Claim 26 depends on claim 123 and recites "wherein the antibody heavy chain variable domain further comprises another framework region, wherein the another framework region comprises an amino acid at amino acid position 91…" This claim has express support in Example 7 at page 141, line 30 to page 142, line 17. Example 7 discloses a library of monobodies where four variants were generated at four framework positions—residues 37, 45, 47, and 91. These residues are the ones particularly claimed in claims 123 and 126. Residues 37, 45, and 47 are in Framework Region 2 and residue 91 is in Framework Region 3 with CDRH2 positioned between the two framework regions.

Thereby, framework region 3 is the "another framework." Framework regions of antibodies are known to those of skill in the art and sequences for the framework regions are publicly available. For at least this reason, Applicant respectfully asserts that "another framework region" is fully supported by the specification.

The examiner has not provided any evidence that one of skill in the art would not have been in possession of at least two framework regions given the disclosure in the specification as well as the knowledge in the art. In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections under 5 U.S.C. § 112, first paragraph.

Rejection under Obviousness-Type Double Patenting

The Examiner provisionally rejects claims 105, 107, 109, 111, 113, 115-122 and 127-128 under the judicially created doctrine of obviousness-type double patenting over claims 22, 25, 26, 30-31, 35-37 and 48-50 of copending Application No. 11/102,502 in view of Sidhu et al. (*J. Mol. Biol.,* 296:487-495 (2000)) and evidenced by Bond et al. (*J. Mol. Biol.,* 332:643-655 (2003)). Applicant acknowledges the Examiner's rejection for obviousness-type double patenting and requests that this rejection be held in abeyance until notice of allowable subject matter.

Interview Request

Applicants request an interview with the examiner and her supervisor upon receipt of these papers.

Summary

Applicant submits that the claims of the present application are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicant's representative at the telephone number listed below, if the Examiner believes that doing so will advance prosecution.

Please charge any additional fees or credit any overpayment to Merchant & Gould P.C., Deposit Account No. 13-2725.

Respectfully submitted,

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Date: May 18, 2009

/Katherine M. Kowalchyk/
Reg. No. 36, 848

23552
PATENT TRADEMARK OFFICE

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ADAN RIOS

Appeal 2009-1967
Application 10/667,534
Technology Center 1600

Decided:[1] March 31, 2009

Before DEMETRA J. MILLS, ERIC GRIMES, and JEFFREY N. FREDMAN, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, begins to run from the decided date shown on this page of the decision. The time period does not run from the Mail Date (paper delivery) or Notification Date (electronic delivery).

STATEMENT OF CASE

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for lack of written description. We have jurisdiction under 35 U.S.C. § 6(b). The following claim is representative.

48. A method of eliciting an immune response comprising:
obtaining a viral particle comprising a reverse transcriptase that has been inactivated by binding said reverse transcriptase with one or more azido-lableled compounds and then irradiating said reverse transcriptase; and
administering the viral particle to a subject, wherein an immune response is elicited in the subject.

Ground of Rejection

Claims 40-50 are rejected under 35 U.S.C. §112, first paragraph for lack of written description.

References Relied on by Appellant

Flavell, "Retroelements, reverse transcriptase and evolution," *Comp. Biochem. Physiol.,* Vol. 110B, No. 1, pp. 3-15 (1995).

Boeke, "The unusual phylogenetic distribution of retrotransposons: A hypothesis," *Genome Res.,* Vol. 13, pp. 1975-1983 (2003).

Nakamura et al., "Telomerase catalytic subunit homologs from fission yeast and human," *Science,* Vol. 277 (August 15, 1997).

Springer et al., "Phylogenetic relationships of reverse transcriptase and Rnase H sequences and aspects of genome structure in the gypsy group of retrotransposons," *Mol. Biol. Evol.,* 10 (6), pp. 1370-1379 (1993).

Lingner et al., "Reverse transcriptase motifs in the catalytic subunit of telomerase," *Science*, Vol. 276, p. 561 (1997).

Valverde-Garduno et al., "Functional analysis of HIV-1 reverse transcriptase motif C: site-directed mutagenesis and metal cation interaction," *J. Mol. Evol.*, 47(1), pp. 73-80 (1988).

Seifarth et al., "Rapid identification of all known retroviral reverse transcriptase sequences with a novel versatile detection assay, AIDS Research and Human Retroviruses," *Aids Research and Human Retroviruses,* Vol. 16, No. 8, pp. 721-729 (2000).

ISSUE

The Examiner argues that the claims are broad and the disclosure fails to teach the inactivation of any other retroviral or retrotransposon reverse transcriptases (RTs) other than HIV-1.

The Applicant argues that

> HIV is a retrovirus and a unique aspect of retrovirus replication is the conversion of a single-stranded RNA from the virus genome into a doublestranded DNA molecule that must integrate into the genome of the host cell prior to the synthesis of viral proteins and nucleic acids (Specification, p. 3, ln. 4-12). Accordingly, all retroviruses possess a reverse transcriptase enzyme, which converts the RNA of their genetic material into DNA (Specification, p. 3, ln. 14-16). Furthermore, since all reverse transcriptases prime the synthesis of new DNA from tRNA, which is a molecule with abundant secondary structure strongly associated with the enzyme, it is generally accepted that the catalytic unit among reverse transcriptases is phylogenetically conserved.

(App. Br. 3.)

The issue is: Has the Examiner shown that the disclosure does not convey with reasonable clarity to those skilled in the art, that the inventor was in possession of the invention, and is there written descriptive support in

the Specification for inactivation of reverse transcriptases generally and for the method of illiciting an immune response, as claimed?

FINDINGS OF FACT

The Examiner finds that:

1. "The claims of the instant application are directed toward a method of eliciting an immune response by obtaining a viral particle comprising a reverse transcriptase (RT) that has been inactivated with one or more azido-labeled compounds followed by irradiation." (Ans. 6.)

2. "The broadest claims are not directed toward any particular source of the RT enzyme. Perusal of the disclosure demonstrates that applicants were clearly focused on HIV-1, in particular for the development of an efficacious vaccine." (Ans. 6.)

3. In summarizing his invention (Spec. p. 2, lines 11-19) [A]pplicants stated the following:

> The present invention relates generally to the fields of virology, immunology, disease treatment, and prevention. More particularly, it concerns HIV particles with inactivated reverse transcriptase, methods of inactivation, and the use of such particles to prepare components of HIV and to elicit effective immunological responses to HIV. These immune responses are useful in producing diagnostic reagents, assays, and kits for the diagnosis of HIV and related retroviral disease, providing protection from an HIV challenge, and assisting an HIV-infected individual in controlling the replication of the virus. Methods of inactivation are useful for preventing disease through decreasing the risk of infection associated with exposure to HIV infected tissues and materials. [p. 2, l. 11-19]

(Ans. 6-7.)

4. "The [S]pecification in describing the related art discusses only HIV." (Ans. 7.)

7. No other retroviruses are described to any extent in the Specification. 5Ans. 7.)

6. "The [S]pecification discusses HIV biology and the worldwide geographic distribution of the virus (pp. 16-18). All of the examples provided in the [S]pecification involve HIV-1 RT (e.g., see Example 1: photoinactivation of HIV-1 RT [p. 30-31; Example 2: inactivation of HIV particles and infected cells [p. 31])." (Ans. 7-8.)

7. There is no mention of any other retroviral or retrotransposon RTs in the Specification. (Ans. 8.)

8. The *Retroviridae* encompass several genera including the avian-leukosis-sarcoma viruses (e.g., Rous sarcoma virus (RSV), avian myeloblastosis virus (AMV), avian erythroblastosis virus (AEV), avian myelocytomatosis virus (MC)), mammalian C-type retroviruses (e.g., Moloney murine leukemia virus (Mo-MLV), Harvey murine sarcoma virus (Ha-MSV), Abelson murine leukemia virus (A-MuLV) , feline leukemia virus (FeLV), reticuloendotheliosis virus (REV), spleen necrosis virus (SNV)), B-type viruses (e. g., Mouse mammary tumor virus (MMTV)) , D-type viruses (e. g., Mason-Pfizer monkey virus (MPMV) , "SAIDS" viruses), HTLV-BLV viruses (e. g., Human T-cell leukemia virus (HTLV-I and -II), Bovine leukemia virus (BLV)), lentiviruses (e.g., human immunodeficiency virus (HIV-1 and -2 simian immunodeficiency virus (SIV), feline immunodeficiency virus (FIV), bovine immunodeficiency virus (BIV), Visna/maedi virus, caprine arthritis-encephalitis virus (CAEV), equine infectious anemia virus (EIAV)), and spumaviruses (e. g., simian foamy virus (SFV), human foamy virus (HFV), human spumaretrovirus (HSRV)). The [S]pecification fails to discuss any other virus other than HIV. Once again, there is no indication that [A]pplicants contemplated inactivating RT from any of the aforementioned viruses except HIV-1.

(Ans. 8.)

9. "The disclosure fails to teach the inactivation of any other retroviral or retrotransposon RTs other than HIV-1." (Ans. 8.)

10. The Examiner concludes that "the skilled artisan would conclude that applicants were not in possession of the full genus claimed." (Ans. 8.)

11. According to the Specification, page 13, the immune response may be a humoral response, a cellular response or both a humoral and cellular response. "The cellular response may be a CD8+ T cell response, a CD4+ T cell, or both a CD8+ T cell and a CD4+ cell response," however, throughout the [S]pecification, the disclosure particularly is directed to a protective immune response to HIV. (Spec. 13.)

12. The Specification, page 16, ll. 20-25 provides that, it is "of importance to note that the methodology of the present invention is applicable to any retrovirus which may be associated with any animal or human disease as a method for development of effective immunogens and preventive vaccines."

13. "In one embodiment the RT is inactivated by one or more compounds that binds the RT and then irradiating bound RT with UV light. . . . . In one embodiment of the compound that binds to RT is an azido labeled compound." (Spec. 12: 8-18.)

14. Lingner, Figs. 2 and 3 evidence that reverse transcriptase domains are shared by multiple reverse transcriptases, with several highly conserved regions. (Lingner, 562.)

PRINCIPLES OF LAW

"[The written description] inquiry is a factual one and must be assessed on a case-by-case basis." *Purdue Pharma L.P. v. Faulding, Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000). The Specification need not describe the invention in the same terms used in the claims, but the disclosure must

convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. See *id.*

The degree of specificity required to adequately describe an invention "varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence." *Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005). *See also id.* at 1359 ("[W]hat is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.") *See, e.g., In re Wallach*, 378 F.3d 1330, 1333-34 (Fed. Cir. 2004) (an amino acid sequence supports "the entire genus of DNA sequences" that can encode the amino acid sequence because "the state of the art has developed" such that it is a routine matter to convert one to the other); *Univ. of Rochester v. G.D. Searle & Co.*, 358 F. 3d 916, 925 Cir. 2004). (considering whether the patent disclosed the compounds necessary to practice the claimed method, given the state of technology); *Singh v. Brake*, 317 F.3d 1334, 1343 (Fed. Cir. 2002) (affirming adequacy of disclosure by distinguishing precedent in which the selection of a particular species within the claimed genus had involved "highly unpredictable results"). Furthermore, an actual reduction to practice is not required for written description. *See Univ. of Rochester v. G.D. Searle & Co.*, 358 F. 3d at 926. This written description requirement applies not only to compositions of matter, but to methods as well. *University of Rochester v. G.D. Searle & Co.*, 358 F.3d at 926.

Claim Interpretation and Claim Scope

Claim 48 is directed to a method of eliciting an immune response comprising: obtaining a viral particle comprising a reverse transcriptase that has been inactivated by binding said reverse transcriptase with one or more azido-labeled compounds and then irradiating said reverse transcriptase; and administering the viral particle to a subject, wherein an immune response is elicited in the subject.

Any immune response is encompassed by the claimed method, which is not limited to protective immune responses. (FF 13.) The claims encompass the use of any viral particle including a reverse transcriptase that has been inactivated by binding the reverse transcriptase with one or more azido-labeled compounds and then irradiated.

ANALYSIS

The Appellant argues that:

> HIV is a retrovirus and a unique aspect of retrovirus replication is the conversion of a single-stranded RNA from the virus genome into a doublestranded DNA molecule that must integrate into the genome of the host cell prior to the synthesis of viral proteins and nucleic acids (Specification, p. 3, ln. 4-12). Accordingly, all retroviruses possess a reverse transcriptase enzyme, which converts the RNA of their genetic material into DNA (Specification, p. 3, ln. 14-16). Furthermore, since all reverse transcriptases prime the synthesis of new DNA from tRNA, which is a molecule with abundant secondary structure strongly associated with the enzyme, it is generally accepted that the catalytic unit among reverse transcriptases is phylogenetically conserved.

(App. Br. 3.)

We conclude that the Examiner has not provided sufficient evidence to show that, in view of the Specification, the skilled artisan would not have

been placed in possession of the method of the claims. In particular, the skilled artisan would have been in possession of the general technique disclosed in the Specification of inactivating HIV reverse transcriptase as applicable to reverse transcriptases generally (*see* FF 11), which share similar conserved structure and catalytic units. Therefore that the Examiner has not shown that the Specification fails to adequately describe the invention of the claims on appeal.

"The 'written description' requirement serves a teaching function, . . . in which the public is given 'meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time.'" *University of Rochester v. G.D. Searle & Co., Inc.* , 358 F.3d 916, 922 (Fed. Cir. 2004) (citation omitted). Another "purpose of the 'written description' requirement is . . . [to] convey with reasonable clarity to those skilled in the art that, as of the filing date [ ], [the applicant] was in possession *of the invention*." *Vas-Cath Inc. v. Mahurkar* , 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). *See also Enzo Biochem Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1329 (Fed. Cir. 2002). The requirement is satisfied when the Specification "set[s] forth enough detail to allow a person of ordinary skill in the art to understand what is claimed and to recognize that the inventor invented what is claimed." *University of Rochester*, 358 F.3d at 928. It is the Examiner's "initial burden [to] present[ ] evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims" (*In re Wertheim*, 541 F.2d 257, 263 (CCPA 1976)). "[A]pplicants have some flexibility in the 'mode selected for compliance' with the written description requirement" (*University of Rochester*, 358 F.3d at 928); it is well settled that actual reduction to practice is not necessary to satisfy the requirement (*id.*, at 926).

Appellant argues that:

> Since retroviruses cannot integrate into the genetic machinery of the host cell without reverse transcription, the inhibition of reverse transcriptase has as a universal consequence on the inability of any retrovirus to integrate within the genetic machinery of a suitable host cell. Thus, regardless of the type of retrovirus, the inactivation of reverse transcriptase as described in the present specification would be understood by a person of ordinary skill in the art to be applicable to any retrovirus. The importance of RT to retroviruses in general, is further evidenced by the number of known anti-retroviral compounds that interfere with RT activity (e.g., AZT [azidothymidine], nevirapine, pyridinones, carboxanilides) (Specification, p. 3, ln. 23 to p. 4, ln. 8).
>
> As described in the present specification, a reverse transcriptase may be inactivated by binding the reverse transcriptase with one or more azido-labeled compounds and then irradiating it (see e.g., p. 12, ln. 8-9). Numerous compounds that bind to reverse transcriptases were known in the art (see e.g., Specification, p. 3, ln. 23, to p. 4, ln. 11).

(App. Br. 4.)

The Examiner finds that "the various exhibits relied upon [by Appellants]... fail to support applicants' arguments," and that nothing in the Specification leads the skilled artisan to a particular retrovirus. (Ans. 9.) We find that Appellant has the better argument.

In our view, the Examiner's own rejection evidences that the skilled artisan would have been in possession of knowledge that the scope of *Retroviridae* encompasses a number of different genera (see Ans. 8). Further, the skilled artisan would have known that all of these well known retrovirus species require active reverse transcriptase activity. The Examiner's statement that "there is no indication that applicants

contemplated inactivating RT from any of the aforementioned viruses except HIV-1" is not correct. Appellants's Specification specifically states that "the methodology of the present invention is applicable to any retrovirus which may be associated with any animal or human disease as a method for development of effective immunogens and preventive vaccines" (Spec. 16, ll. 20-25; FF 12). This quotation from the Specification cannot be read as anything other than a direct teaching to apply the claimed inactivation method to known retrovriuses that are assocaited with human or animal disease. At the very least, this teaching places the skilled artisan in possession of the claimed method with known pathogenic or zoonotic retroviruses.

The Examiner has not provided adequate evidence that the skilled artisan would not have been in possession of known retroviruses. The Examiner has also not adequately addressed Appellant's argument that one of ordinary skill in the art would have understood from the conserved regions and similarity of function of reverse transcriptases generally, that they could be predictably inactivated using azido-labeled compounds and irradiation and used in the claimed method.

The evidence of record supports the Specification's description of the disclosed method as applicable to retroviruses generally, rather than applicable only to HIV. In other words, the Examiner has not provided evidence that one of ordinary skill in the art would not have understood that azido compounds bind to reverse transcriptases generally, and that one of ordinary skill in the art would not have expected that irradiated azido-labeled compounds inactivate reverse transcriptases generally.

In view of the above, we find that the Examiner has not shown that the disclosure does not convey with reasonable clarity to those skilled in the

art, that the inventor was in possession of the invention. The written description rejection is reversed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

REVERSED

Ssc:

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